

=> b reg

FILE 'REGISTRY' ENTERED AT 16:46:12 ON 24 OCT 2006

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STRUCTURE FILE UPDATES: 23 OCT 2006 HIGHEST RN 911100-17-9

DICTIONARY FILE UPDATES: 23 OCT 2006 HIGHEST RN 911100-17-9

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

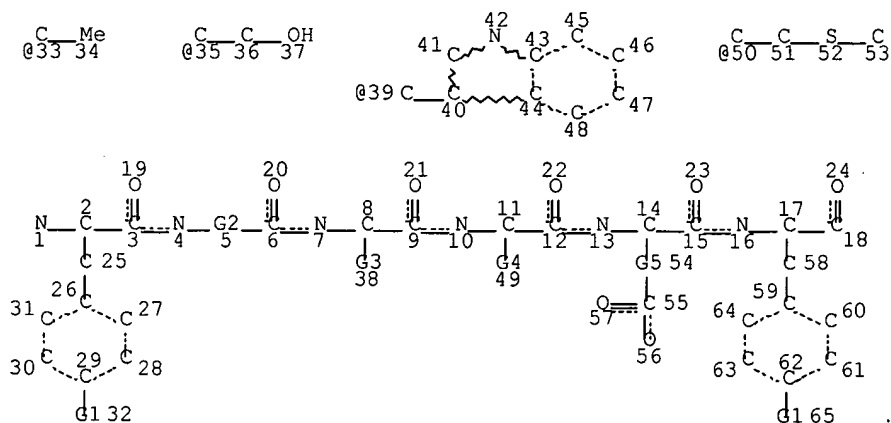
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<http://www.cas.org/ONLINE/UG/regprops.html>

=> d que sta l11

L9 STR



VAR G1=H/OH

VAR G2=C/33/35

VAR G3=I-PR/S-BU/39

VAR G4=I-BU/50

REP G5=(1-2) C

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 1

CONNECT IS M1 RC AT 18

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 65

STEREO ATTRIBUTES: NONE

L11 236 SEA FILE=REGISTRY CSS FUL L9

100.0% PROCESSED 395878 ITERATIONS  
SEARCH TIME: 00.00.08

236 ANSWERS

=> => d que sta l14

L14 216 SEA FILE=REGISTRY ABB=ON PLU=ON (GPWLEEEEEAY)|(LGPQGPPHLVADPS  
KKQGPWLEEEEEAY)/SQSP

=> d que sta l17

L17 12 SEA FILE=REGISTRY ABB=ON PLU=ON 'GLP'GPWLEEEEEAYGWLDF/SQSP

=> => b hcap

FILE 'HCAPLUS' ENTERED AT 17:12:21 ON 24 OCT 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 24 Oct 2006 VOL 145 ISS 18

FILE LAST UPDATED: 23 Oct 2006 (20061023/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitind hitrn fhitstr l59 tot

L59 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:30988 HCAPLUS Full-text

DN 144:127491

TI Combination therapy of diabetes

IN Cruz, Antonio

PA Waratah Pharmaceuticals, Inc., Can.

SO PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO2006002532	A1	20060112	2005WO-CA01024	20050629
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRAI 2004US-584635P P 20040701

AB The authors disclose combination therapy for diabetes comprising CD3 antibodies, gastrins, and glucagon-like peptide-1 (GLP-1) receptor agonists.

IC ICM C07K-0019/00  
ICS A61K-0038/22; A61P-0003/10; A61K-0038/26; A61K-0039/395;  
A61K-0048/00; C07K-0016/28; C07K-0014/595; A61K-0038/16

CC 15-3 (Immunochemistry)  
Section cross-reference(s): 2, 14

IT **Antidiabetic agents**  
Combination chemotherapy  
Human  
Immunotherapy  
(CD3 agonists in combination with gastrins for diabetes therapy)

IT **Hyperglycemia**  
(CD3 agonists in combination with gastrins for diabetes therapy in relation to amelioration of OKT3)

IT **Pancreatic islet of Langerhans**  
(allotransplant; CD3 agonists in combination with gastrins for diabetes therapy in relation to)

IT **Diabetes mellitus**  
(insulin-dependent; CD3 agonists in combination with gastrins for therapy of)

IT **Diabetes mellitus**  
(non-insulin-dependent, LADA (latent autoimmune diabetes in adult); CD3 agonists in combination with gastrins for therapy of)

IT **Pancreatic islet of Langerhans**  
( $\beta$ -cell; CD3 agonists in combination with gastrins for diabetes therapy in relation to function of)

IT 1947-37-1, Tetragastrin 5534-95-2, Pentagastrin 10047-33-3,  
Human gastrin 17 I 39024-57-2 60675-77-6, Human gastrin-34 I  
70706-59-1, Gastrin-14 I (human) 82800-54-2 143572-94-5  
696646-41-0 862148-47-8, Gastrin 71 (human) 862148-48-9,  
Gastrin 52 (human)  
RL: THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)  
(CD3 agonists in combination with gastrins for diabetes therapy in relation to amelioration of OKT3)

IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(CD3 agonists in combination with gastrins for diabetes therapy in relation to production of)

IT 107444-51-9 873133-86-9 873133-87-0 873133-89-2  
873133-90-5 873133-91-6 873133-92-7 873133-93-8 873133-94-9  
873133-95-0 873133-96-1 873133-97-2 873133-98-3 873341-25-4  
873341-26-5  
RL: PRP (Properties)  
(unclaimed protein sequence; combination therapy of diabetes)

IT 35144-91-3 106612-94-6, 7-37-Glucagon-like peptide I (human)  
123475-27-4 305790-37-8 308349-05-5 560114-83-2 862539-16-0  
873097-66-6  
RL: PRP (Properties)  
(unclaimed sequence; combination therapy of diabetes)

IT 10047-33-3, Human gastrin 17 I 39024-57-2  
70706-59-1, Gastrin-14 I (human) 143572-94-5  
696646-41-0  
RL: THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)  
(CD3 agonists in combination with gastrins for diabetes therapy in relation to amelioration of OKT3)

IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(CD3 agonists in combination with gastrins for diabetes therapy in relation to production of)

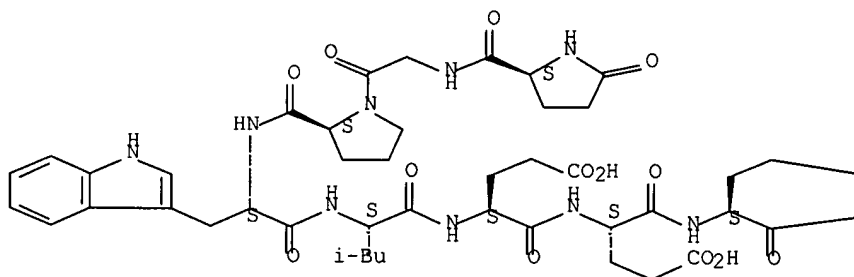
IT 107444-51-9  
RL: PRP (Properties)  
(unclaimed protein sequence; combination therapy of diabetes)

IT 106612-94-6, 7-37-Glucagon-like peptide I (human)  
873097-66-6

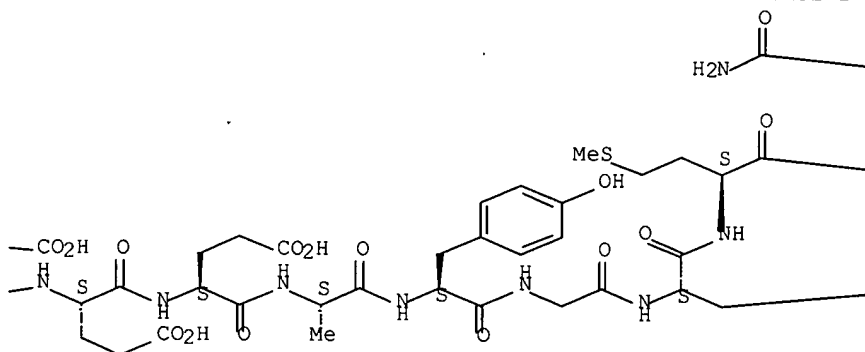
RL: PRP (Properties)  
 (unclaimed sequence; combination therapy of diabetes)  
 IT 10047-33-3, Human gastrin 17 I  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CD3 agonists in combination with gastrins for diabetes therapy in  
 relation to amelioration of OKT3)  
 RN 10047-33-3 HCAPLUS  
 CN Gastrin-17 I (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

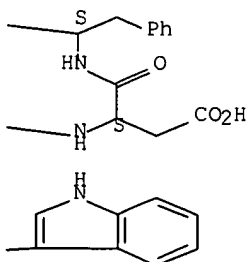
PAGE 1-A



PAGE 1-B



PAGE 1-C



RE.CNT 8      THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN  
AN 2005:732490 HCAPLUS Full-text  
DN 143:223078  
TI Combined use of a GLP-1 agonist and gastrin compounds  
IN Cruz, Antonio; Pastrak, Aleksandra; Hew, Yin  
PA Waratah Pharmaceuticals, Inc., Can.  
SO PCT Int. Appl., 55 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO2005072045	A2	20050811	2005WO-CA00099	20050128
	WO2005072045	A3	20051027		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU2005207870	A1	20050811	2005AU-0207870	20050128
	CA---2554458	AA	20050811	2005CA-2554458	20050128
	EP---1711532	A2	20061018	2005EP-0706425	20050128
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
PRAI	2004US-540803P	P	20040130		
	2004US-540804P	P	20040130		
	2005WO-CA00099	W	20050128		

AB The invention relates to compns., conjugates, and methods for the prevention and/or treatment of a condition and/or disease comprising a therapeutically effective amount of a GLP-1 agonist and a gastrin compound The combination of a GLP-1 agonist and a gastrin compound provides beneficial effects, in particular sustained beneficial effects, in the prevention and/or treatment of conditions and/or diseases for which either a GLP-1 agonist or a gastrin compound have been demonstrated to have a therapeutic effect, including but not limited to diabetes, hypertension, chronic heart failure, fluid retentive states, obesity, metabolic syndrome and related diseases and disorders. Combinations of a GLP-1 agonist and a gastrin compound can be selected to provide unexpectedly additive effects or synergistic effects.

IC ICM A61K  
CC 2-6 (Mammalian Hormones)  
IT Alzheimer's disease  
Anti-Alzheimer's agents  
Antiarrhythmics  
Antiulcer agents  
Bacteremia  
Dyspepsia  
Gastrointestinal agents  
Human

**Hyperglycemia**

Hypoglycemia

Respiratory distress syndrome

Septicemia

(combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT **Antidiabetic agents**  
Antihypertensives  
Antiobesity agents  
Cardiovascular agents

Combination chemotherapy  
 Diabetes mellitus  
 Drug delivery systems  
 Hypertension  
 Obesity  
 (combined therapeutic use of GLP-1 agonists and gastrin compds.)

IT Morphogenesis, animal  
 Pancreatic islet of Langerhans  
 (method of inducing islet neogenesis; combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT Albumins, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (serum, human, gastrin compound is associated with serum protein; combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT 1947-37-1, Tetragastrin 5534-95-2, Pentagastrin 9002-76-0, Gastrin 9002-76-0D, Gastrin, compds. 10047-33-3, Gastrin-17 I (human) 20994-88-1 22655-78-3, 2-17-Human gastrin I 39024-57-2 60675-77-6, Gastrin-34 I (human) 70706-59-1, Gastrin-14 I (human) 70741-94-5 82800-54-2 87805-34-3, Glucagon-like peptide I (human) 87805-34-3D, Glucagon-like peptide I (human), fragments, analogs, derivs., metabolites, and prodrugs 89750-14-1, Glucagon-like peptide I 107444-51-9, 7-36-Glucagon-like peptide 1 amide 107444-51-9D, 7-36-Glucagon-like peptide 1 amide, fragments, analogs, derivs., metabolites, and prodrugs 123475-27-4 194551-05-8 224638-84-0 227472-22-2 258289-68-8 381729-75-5 381729-76-6 381729-78-8 381729-99-3 435276-95-2 435276-96-3 496765-91-4 577758-23-7 577758-44-2 862415-61-0 862415-63-2 862415-64-3  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT 59112-80-0, C-Peptide  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (therapeutic combination increases C-peptide production; combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT 9004-10-8, Insulin, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (therapeutic combination increases insulin production; combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT 50-99-7, D-Glucose, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (therapeutic combination normalizes blood glucose levels; combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT 35144-91-3 143572-94-5 560114-83-2 696646-41-0 862539-16-0  
 RL: PRP (Properties)  
 (unclaimed sequence; combined use of GLP-1 agonist and gastrin compds.)

IT 10047-33-3, Gastrin-17 I (human) 20994-88-1 22655-78-3, 2-17-Human gastrin I 39024-57-2 70706-59-1, Gastrin-14 I (human) 70741-94-5 107444-51-9, 7-36-Glucagon-like peptide 1 amide 107444-51-9D, 7-36-Glucagon-like peptide 1 amide, fragments, analogs, derivs., metabolites, and prodrugs 862415-61-0 862415-63-2 862415-64-3  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT 59112-80-0, C-Peptide  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (therapeutic combination increases C-peptide production; combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT 9004-10-8, Insulin, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (therapeutic combination increases insulin production; combined therapeutic use of GLP-1 agonist and gastrin compds.)

IT 50-99-7, D-Glucose, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(therapeutic combination normalizes blood glucose levels; combined  
therapeutic use of GLP-1 agonist and gastrin compds.)

IT 143572-94-5 696646-41-0

RL: PRP (Properties)

(unclaimed sequence; combined use of GLP-1 agonist and gastrin compds.)

IT 10047-33-3, Gastrin-17 I (human)

RL: PAC (Pharmacological activity); THU (Therapeutic  
use); BIOL (Biological study); USES (Uses)

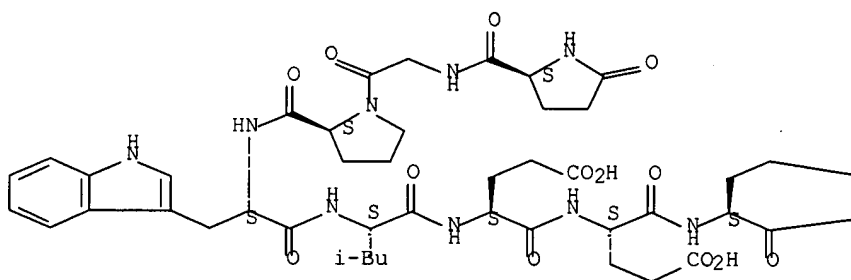
(combined therapeutic use of GLP-1 agonist and gastrin compds.)

RN 10047-33-3 HCAPLUS

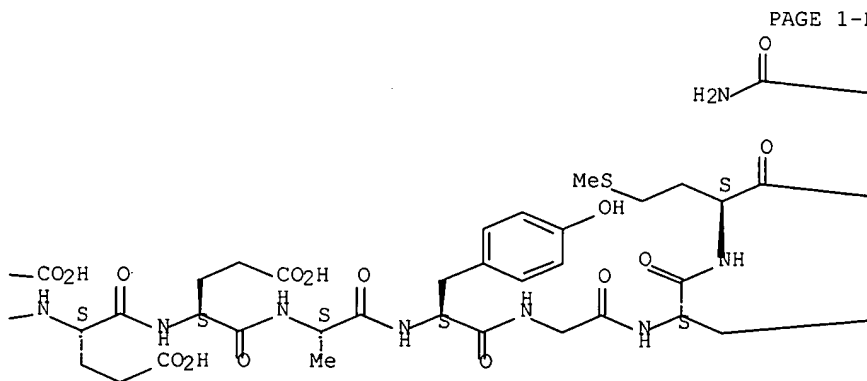
CN Gastrin-17 I (human) (9CI) (CA INDEX NAME)

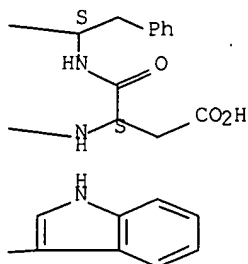
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





L59 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:494650 HCAPLUS Full-text

DN 143:110140

TI Combination therapy with epidermal growth factor and gastrin induces neogenesis of human islet  $\beta$ -cells from pancreatic duct cells and an increase in functional  $\beta$ -cell mass

AU Suarez-Pinzon, Wilma L.; Lakey, Jonathan R. T.; Brand, Stephen J.; Rabinovitch, Alex

CS Department of Medicine, University of Alberta, Edmonton, T6G 2S2, Can.

SO Journal of Clinical Endocrinology and Metabolism (2005), 90(6), 3401-3409  
CODEN: JCEMAZ; ISSN: 0021-972X

PB Endocrine Society

DT Journal

LA English

AB Pancreatic islet transplantation is a viable treatment for type 1 diabetes, but is limited by human donor tissue availability. The combination of epidermal growth factor (EGF) and gastrin induces islet  $\beta$ -cell neogenesis from pancreatic exocrine duct cells in rodents. In this study we investigated whether EGF and gastrin could expand the  $\beta$ -cell mass in adult human isolated islets that contain duct as well as endocrine cells. Human islet cells were cultured for 4 wk in serum-free medium (control) or in medium with EGF (0.3  $\mu$ g/mL), gastrin (1.0  $\mu$ g/mL), or the combination of EGF and gastrin.  $\beta$ -Cell nos. were increased in cultures with EGF plus gastrin (+118%) and with EGF (+81%), but not in cultures with gastrin (-3%) or control medium (-62%). After withdrawal of EGF and gastrin and an addnl. 4 wk in control medium,  $\beta$ -cell nos. continued to increase only in cultures previously incubated with both EGF and gastrin (+232%). EGF plus gastrin also significantly increased cytokeratin 19-pos. duct cells (+678%) in the cultures. Gastrin, alone or in combination with EGF, but not EGF alone, increased the expression of pancreatic and duodenal homeobox factor-1 as well as insulin and C peptide in the cytokeratin 19-pos. duct cells. Also, EGF plus gastrin significantly increased  $\beta$ -cells and insulin content in human islets implanted in immunodeficient nonobese diabetic-severe combined immune deficiency mice as well as insulin secretory responses of the human islet grafts to glucose challenge. In conclusion, combination therapy with EGF and gastrin increases  $\beta$ -cell mass in adult human pancreatic islets in vitro and in vivo, and this appears to result from the induction of  $\beta$ -cell neogenesis from pancreatic exocrine duct cells.

CC 2-10 (Mammalian Hormones)

IT **Keratins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(19; EGF and gastrin combination therapy induction of human islet  
 $\beta$ -cells neogenesis from pancreatic duct cells and increase in  
functional  $\beta$ -cell mass)

IT Cell differentiation

Combination chemotherapy

**Diabetes mellitus**

Human

Transplant and Transplantation

(EGF and gastrin combination therapy induction of human islet  
 $\beta$ -cells neogenesis from pancreatic duct cells and increase in



functional  $\beta$ -cell mass)

IT **Pancreatic islet of Langerhans**  
 ( $\beta$ -cell; EGF and gastrin combination therapy induction of human islet  $\beta$ -cells neogenesis from pancreatic duct cells and increase in functional  $\beta$ -cell mass)

IT 9004-10-8, Insulin, biological studies 59112-80-0, Proinsulin C-peptide  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (EGF and gastrin combination therapy induction of human islet  $\beta$ -cells neogenesis from pancreatic duct cells and increase in functional  $\beta$ -cell mass)

IT 39024-57-2, 15-L-Leucine-human gastrin I 62229-50-9, Epidermal growth factor  
 RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; BIOL (Biological study) (EGF and gastrin combination therapy induction of human islet  $\beta$ -cells neogenesis from pancreatic duct cells and increase in functional  $\beta$ -cell mass)

IT 9004-10-8, Insulin, biological studies 59112-80-0, Proinsulin C-peptide  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (EGF and gastrin combination therapy induction of human islet  $\beta$ -cells neogenesis from pancreatic duct cells and increase in functional  $\beta$ -cell mass)

IT 39024-57-2, 15-L-Leucine-human gastrin I  
 RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; BIOL (Biological study) (EGF and gastrin combination therapy induction of human islet  $\beta$ -cells neogenesis from pancreatic duct cells and increase in functional  $\beta$ -cell mass)

IT 9004-10-8, Insulin, biological studies  
 RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)** (EGF and gastrin combination therapy induction of human islet  $\beta$ -cells neogenesis from pancreatic duct cells and increase in functional  $\beta$ -cell mass)

RN 9004-10-8 HCAPLUS  
 CN Insulin (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L59 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:2163 HCAPLUS Full-text

DN 142:87001

TI Methods for the preparation of pharmaceutical compositions with a gastrin compound having an extended activity and therapeutic uses thereof

IN **Cruz, Antonio**

PA Can.

SO U.S. Pat. Appl. Publ., 25 pp., Cont.-in-part of U.S. Ser. No. 691,123.  
 CODEN: USXXCO

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US2004266682	A1	20041230	2003US-0719450	20031121 <--
	US2004209801	A1	20041021	2003US-0691123	20031022 <--
PRAI	2002US-420187P	P	20021022	<--	
	2002US-420399P	P	20021022	<--	
	2002US-428100P	P	20021121	<--	
	2002US-428562P	P	20021122	<--	
	2002US-430590P	P	20021203	<--	

2003US-0691123            A2     20031022 <--  
2003US-519933P            P     20031114

OS   MARPAT 142:87001

AB   An embodiment of the invention provided herein is a pharmaceutical composition comprising a gastrin compound having an extended activity upon administration to a subject in comparison with native gastrin. Methods are provided of conjugating portions of the amino acid sequence of gastrin having functional ability to bind to the gastrin/CCK receptor, to various carrier moieties, including the use of amino acid spacer regions, and use of bifunctional crosslinking reagents. Methods of treating a diabetes patient with the compns. are provided.

IC   ICM   A61K-0038/22  
ICS   A61K-0038/10; A61K-0038/08

INCL 514012000; 514013000; 514014000; 514015000; 514016000; 530324000;  
530325000; 530326000; 530327000; 530328000

CC   2-10 (Mammalian Hormones)  
Section cross-reference(s): 63

IT   **Antidiabetic agents**  
Immunosuppressants  
(further comprised in gastrin composition; methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   **Diabetes mellitus**  
Drug delivery systems  
Human  
Protein sequences  
(methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   **Pancreatic islet of Langerhans**  
(neogenesis, effect of gastrin-based treatment on; methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   50-99-7, D-Glucose, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood level, effect of gastrin-based treatment on; methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(dependency and sensitivity, effect of gastrin-based treatment on; methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   9002-76-0, Gastrin 10047-33-3, Gastrin-17 I (human)    51165-61-8  
60675-77-6, Gastrin-34 I (human)    818376-84-0    818376-85-1    818376-86-2  
818376-87-3  
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   818376-88-4 818376-89-5    818385-69-2  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   143572-94-5    560114-83-2    696646-41-0  
794567-48-9 794567-49-0  
RL: PRP (Properties)  
(unclaimed sequence; methods for the preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   50-99-7, D-Glucose, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood level, effect of gastrin-based treatment on; methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT   9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(dependency and sensitivity, effect of gastrin-based treatment on; methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT 10047-33-3, Gastrin-17 I (human)  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

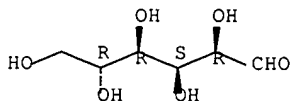
IT 818376-88-4 818376-89-5  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
 (methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT 143572-94-5 696646-41-0 794567-48-9 794567-49-0  
 RL: PRP (Properties)  
 (unclaimed sequence; methods for the preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

IT 50-99-7, D-Glucose, biological studies  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use)  
 (blood level, effect of gastrin-based treatment on; methods for preparation of pharmaceutical compns. with a gastrin compound having an extended activity and therapeutic uses thereof)

RN 50-99-7 HCAPLUS  
 CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:995764 HCAPLUS Full-text

DN 141:420614

TI Gastrin compositions and formulations, and methods of use and preparation

IN Cruz, Antonio

PA Can.

SO U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S. Ser. No. 691,123.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US2004229810	A1	20041118	2003US-0728082	20031203 <--
	US2004209801	A1	20041021	2003US-0691123	20031022 <--
PRAI	2002US-420187P	P	20021022	<--	
	2002US-420399P	P	20021022	<--	
	2002US-428100P	P	20021121	<--	
	2002US-428562P	P	20021122	<--	
	2002US-430590P	P	20021203	<--	
	2003US-0691123	A2	20031022	<--	

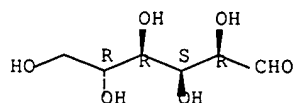
OS MARPAT 141:420614

AB An embodiment of the invention provided herein is a pharmaceutical composition comprising a gastrin compound having an extended activity upon administration to a subject in comparison with native gastrin. Methods are provided of conjugating portions of the amino acid sequence of gastrin having functional ability to bind to the gastrin/CCK receptor, to various carrier moieties, including the use of amino acid

spacer regions, and use of bifunctional crosslinking reagents. Methods of treating a diabetes patient with the compns. are provided.

- IC ICM A61K-0038/10  
ICS A61K-0038/08; C07K-0007/08; C07K-0007/06
- INCL 514014000; 514016000; 514017000; 530326000; 530327000; 530328000;  
530329000; 514015000
- CC 2-6 (Mammalian Hormones)  
Section cross-reference(s): 63
- IT **Antidiabetic agents**  
Human  
Immunosuppressants  
Linking agents  
Molecular cloning  
Protein sequences  
(gastrin compns. and formulations, and methods of use and preparation)
- IT **Diabetes mellitus**  
(insulin-dependent; gastrin compns. and formulations, and methods of use and preparation)
- IT **Pancreatic islet of Langerhans**  
(neogenesis of; gastrin compns. and formulations, and methods of use and preparation)
- IT 50-99-7, D-Glucose, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood, measurement of; gastrin compns. and formulations, and methods of use and preparation)
- IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(dependency upon; gastrin compns. and formulations, and methods of use and preparation)
- IT 143572-94-5DP, conjugates 560114-83-2DP, conjugates  
696646-41-0DP, conjugates 794567-48-9DP, conjugates  
794567-49-0DP, conjugates 795101-07-4DP, conjugates  
795101-08-5DP, conjugates  
RL: BPN (Biosynthetic preparation); **PAC (Pharmacological activity)**  
; PKT (Pharmacokinetics); PNU (Preparation, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study);  
PREP (Preparation); USES (Uses)  
(gastrin compns. and formulations, and methods of use and preparation)
- IT 50-99-7, D-Glucose, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood, measurement of; gastrin compns. and formulations, and methods of use and preparation)
- IT 9004-10-8, Insulin, biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(dependency upon; gastrin compns. and formulations, and methods of use and preparation)
- IT 143572-94-5DP, conjugates 696646-41-0DP, conjugates  
794567-48-9DP, conjugates 794567-49-0DP, conjugates  
RL: BPN (Biosynthetic preparation); **PAC (Pharmacological activity)**  
; PKT (Pharmacokinetics); PNU (Preparation, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study);  
PREP (Preparation); USES (Uses)  
(gastrin compns. and formulations, and methods of use and preparation)
- IT 50-99-7, D-Glucose, biological studies  
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**  
(blood, measurement of; gastrin compns. and formulations, and methods of use and preparation)
- RN 50-99-7 HCAPLUS
- CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:453051 HCAPLUS Full-text

DN 141:12314

TI Gastrin formulations for diabetes treatment

IN Cruz, Antonio

PA Waratah Pharmaceuticals, Inc., Can.

SO PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO2004045640	A1	20040603	2003WO-CA01778	20031121 <--	
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW		
	RW:			BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
	CA---2505167	AA	20040603	2003CA-2505167	20031121 <--	
	AU2003285229	A1	20040615	2003AU-0285229	20031121 <--	
	EP---1565212	A1	20050824	2003EP-0778179	20031121 <--	
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK		
	BR2003016489	A	20051011	2003BR-0016489	20031121 <--	
	CN---1738644	A	20060222	CN 2003-80108818	20031121 <--	
	JP2006513719	T2	20060427	2004JP-0570257	20031121 <--	
	NO2005003027	A	20050822	2005NO-0003027	20050620 <--	
PRAI	2002US-428100P	P	20021121	<--		
	2002US-428562P	P	20021122	<--		
	2002US-430590P	P	20021203	<--		
	2003US-519933P	P	20031114			
	2003WO-CA01778	W	20031121			

OS MARPAT 141:12314

AB An embodiment of the invention provided is a pharmaceutical composition comprising a gastrin compound having an extended activity upon administration to a subject in comparison with native gastrin. Methods are provided of conjugating portions of the amino acid sequence of gastrin having functional ability to bind to the gastrin/CCK<sub>1</sub> receptor, to various carrier moieties, including the use of amino acid spacer regions, and use of bifunctional crosslinking reagents. Methods of treating a diabetes patient with the compns. are provided. Thus, gastrin peptides modified with Cys at the N-terminal were incubated for 30 min with tris[2-carboxyethyl]phosphine-HCl. A molar excess of maleimide-mPEG was conjugated with the above peptide and the conjugate obtained was purified by anion-exchange chromatog.

IC ICM A61K-0039/385

ICS C07K-0014/595; A61K-0038/00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 2

IT **Antidiabetic agents**

Bacillus (bacterium genus)

Crosslinking agents

**Diabetes mellitus**

Drug delivery systems

Escherichia  
Eubacteria  
Human  
Immunosuppressants  
Kluyveromyces  
Pichia  
Saccharomyces  
Schizosaccharomyces  
Streptomyces  
Yeast

(gastrin formulations for diabetes treatment)

IT **Albumins, biological studies**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(serum; gastrin formulations for diabetes treatment)

IT **50-99-7, D-Glucose, biological studies**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood; gastrin formulations for diabetes treatment)

IT 9004-54-0DP, Dextran, reaction products with gastrin compds.  
25322-68-3DP, Polyethylene glycol, reaction products with gastrin compds.  
66009-14-1DP, reaction products with peptide linkers or polymers  
80161-82-6DP, reaction products with peptide linkers or polymers  
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL  
(Biological study); PREP (Preparation); USES (Uses)

(gastrin formulations for diabetes treatment)

IT 1947-37-1, 4-7-Cholecystokinin-7 (swine) 9002-76-0, Gastrin  
10047-33-3, Gastrin-17 I (human) 39024-57-2 66009-14-1  
80161-82-6 82800-54-2 143572-94-5 560114-83-2D,  
reaction products with gastrin compds. 696646-41-0 697288-86-1  
697288-88-3

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)  
(gastrin formulations for diabetes treatment)

IT **50-99-7, D-Glucose, biological studies**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(blood; gastrin formulations for diabetes treatment)

IT 80161-82-6DP, reaction products with peptide linkers or polymers  
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL  
(Biological study); PREP (Preparation); USES (Uses)

(gastrin formulations for diabetes treatment)

IT 10047-33-3, Gastrin-17 I (human) 39024-57-2  
80161-82-6 143572-94-5 696646-41-0

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)  
(gastrin formulations for diabetes treatment)

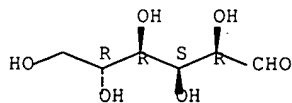
IT **50-99-7, D-Glucose, biological studies**

RL: **THU (Therapeutic use)**; **THU (Therapeutic use)**  
(blood; gastrin formulations for diabetes treatment)

RN 50-99-7 HCAPLUS

CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L59 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:368884 HCAPLUS Full-text

DN 140:386447

TI Methods and composition for the treatment of diabetes with FACGINT (Factor  
for Complementing Gastrin for Islet Neogenesis Therapy)

IN Brand, Stephen J.; Cruz, Antonio; Pastrak, Aleksandra; Hew, Yin

PA Waratah Pharmaceuticals, Inc., Can.

SO PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DT Patent  
LA English  
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO2004037195	A2	20040506	2003WO-US33595	20031022 <--
	WO2004037195	A3	20050616		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA---2501677	AA	20040506	2003CA-2501677	20031022 <--
	AU2003283004	A1	20040513	2003AU-0283004	20031022 <--
	BR2003015523	A	20050830	2003BR-0015523	20031022 <--
	EP---1569680	A2	20050907	2003EP-0774936	20031022 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
	CN---1729016	A	20060201	CN 2003-80107284	20031022 <--
	JP2006506386	T2	20060223	2004JP-0547077	20031022 <--
	NO2005002419	A	20050707	2005NO-0002419	20050519 <--
	US2006189520	A1	20060824	2006US-0532295	20060217 <--
PRAI	2002US-420187P	P	20021022	<--	
	2002US-420399P	P	20021022	<--	
	2002US-428100P	P	20021121	<--	
	2002US-428562P	P	20021122	<--	
	2003WO-US33595	W	20031022		
AB	Compns. and methods are provided for islet neogenesis therapy comprising a member of a group of factors that complement a gastrin/CCK receptor ligand, with formulations, devices and methods for sustained release delivery and for local delivery to target organs. Methods and composition for the transplantation of stem cells and stimulation to proliferate and differentiated into insulin-producing cells are also claimed.				
IC	ICM A61K				
CC	2-6 (Mammalian Hormones)				
IT	<b>Antidiabetic agents</b> (FACGINT; methods and composition for treatment of diabetes with FACGINT (Factor for Complementing Gastrin for Islet Neogenesis Therapy))				
IT	<b>Diabetes mellitus</b> Drug delivery systems Drug toxicity Human Immunosuppressants Immunosuppression (methods and composition for treatment of diabetes with FACGINT (Factor for Complementing Gastrin for Islet Neogenesis Therapy))				
IT	<b>Pancreatic islet of Langerhans</b> (neogenesis; methods and composition for treatment of diabetes with FACGINT (Factor for Complementing Gastrin for Islet Neogenesis Therapy))				
IT	Embryo, animal <b>Pancreatic islet of Langerhans</b> Umbilical cord (stem cells transplantation and differentiation into insulin-producing cells; methods and composition for treatment of diabetes with FACGINT (Factor for Complementing Gastrin for Islet Neogenesis Therapy))				
IT	<b>Pancreatic islet of Langerhans</b> ( $\beta$ -cell, mass in response to treatment; methods and composition for treatment of diabetes with FACGINT (Factor for Complementing Gastrin for Islet Neogenesis Therapy))				
IT	50-99-7, Glucose, biological studies RL: BSU (Biological study, unclassified); BIOL (Biological study)				

(blood and serum levels in response to treatment; methods and composition for treatment of diabetes with FACGINT (Factor for Complementing Gastrin for Islet Neogenesis Therapy))

IT 1393-25-5, Secretin 9002-62-4, Prolactin, biological studies  
 9002-72-6, Somatotropin 9061-61-4, NGF 11096-26-7, Erythropoietin  
 37221-79-7, VIP 59392-49-3, Gastric inhibitory polypeptide  
 61912-98-9, IGF 62031-54-3, Fibroblast growth factor  
 83869-56-1, Granulocyte-macrophage colony stimulating factor 89750-14-1,  
 Glucagon-like peptide I 89750-15-2, Glucagon-like peptide 2  
 103370-86-1, Parathormone-related peptide 104625-48-1, Activin-A  
 127464-60-2, Vascular endothelial growth factor 137061-48-4, Pituitary  
 adenylate cyclase-activating polypeptide 143011-72-7, Granulocyte colony  
 stimulating factor 148348-15-6, Fibroblast growth factor 7  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological  
 activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (co-treatment with FACGINT; methods and composition for treatment of  
 diabetes with FACGINT (Factor for Complementing Gastrin for Islet  
 Neogenesis Therapy))

IT 9002-76-0, Gastrin 39024-57-2 60748-06-3, Gastrin-17  
 RL: PAC (Pharmacological activity); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
 (methods and composition for treatment of diabetes with FACGINT (Factor for  
 Complementing Gastrin for Islet Neogenesis Therapy))

IT 9004-10-8, Insulin, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (serum and pancreas levels in response to treatment; methods and composition  
 for treatment of diabetes with FACGINT (Factor for Complementing Gastrin  
 for Islet Neogenesis Therapy))

IT 50-99-7, Glucose, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (blood and serum levels in response to treatment; methods and composition  
 for treatment of diabetes with FACGINT (Factor for Complementing Gastrin  
 for Islet Neogenesis Therapy))

IT 59392-49-3, Gastric inhibitory polypeptide 61912-98-9,  
 IGF  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological  
 activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (co-treatment with FACGINT; methods and composition for treatment of  
 diabetes with FACGINT (Factor for Complementing Gastrin for Islet  
 Neogenesis Therapy))

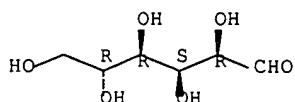
IT 39024-57-2  
 RL: PAC (Pharmacological activity); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
 (methods and composition for treatment of diabetes with FACGINT (Factor for  
 Complementing Gastrin for Islet Neogenesis Therapy))

IT 9004-10-8, Insulin, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (serum and pancreas levels in response to treatment; methods and composition  
 for treatment of diabetes with FACGINT (Factor for Complementing Gastrin  
 for Islet Neogenesis Therapy))

IT 50-99-7, Glucose, biological studies  
 RL: PAC (Pharmacological activity); THU (Therapeutic  
 use)  
 (blood and serum levels in response to treatment; methods and composition  
 for treatment of diabetes with FACGINT (Factor for Complementing Gastrin  
 for Islet Neogenesis Therapy))

RN 50-99-7 HCAPLUS  
 CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.





L59 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:162205 HCAPLUS Full-text  
 DN 140:205102  
 TI Treatment for diabetes  
 IN Brand, Stephen J.; Cruz, Antonio; Rabinovitch, Alex;  
 Suarez-Pinzon, Wilma Lucia  
 PA Waratah Pharmaceuticals, Inc., USA  
 SO U.S. Pat. Appl. Publ., 31 pp., Cont.-in-part of U.S. Ser. No. 29,551.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US2004037818	A1	20040226	2003US-0446612	20030527
	WO---9519785	A1	19950727	1993WO-US12055	19940124
	W: AU, CA, JP, KR, RU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU---9476287	A1	19950808	1994AU-0076287	19940124
	JP--09511384	T2	19971118	1995JP-0519519	19940124
	EP---1132091	A1	20010912	2001EP-0114131	19940124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	AT---222503	E	20020915	1994AT-0926459	19940124
	ES---2185663	T3	20030501	1994ES-0926459	19940124
	EP---1466618	A1	20041013	2004EP-0076250	19940124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	US---6288301	B1	20010911	1998US-0127028	19980730
	US---6558952	B1	20030506	1999US-0241100	19990129
	US2002081285	A1	20020627	2001US-0029551	20011220
	JP2005087209	A2	20050407	2004JP-0234827	20040811
PRAI	1998US-0127028	A2	19980730		
	1999US-0241100	A1	19990129		
	2001US-0029551	A2	20011220		
	2002US-382921P	P	20020524		
	2002US-384357P	P	20020530		
	1992US-0992255	A1	19921214		
	1994EP-0926459	A3	19940124		
	2001EP-0114131	A3	19940124		
	1995JP-0519519	A3	19940124		
	1993WO-US12055	W	19940124		

AB Proliferating pancreatic islet cells are disclosed that are obtained by the method of isolating a population of cells that preferably includes predominantly islet precursor cells that express one or more markers associated with an islet precursor cell and providing the precursor cells with one or more a pancreatic differentiation agent so that a population of cells is obtained that has a high proportion of cells with phenotypic characteristics of functional pancreatic islet  $\beta$ -cells. Optionally, the precursor cells are pretreated by providing them with one or more cell expansion agents to increase the number of cells in the population prior to differentiation. The pancreatic differentiation agent composition comprises a gastrin/CCK receptor ligand, e.g., a gastrin, in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells. The cell expansion agent composition comprises one or more epidermal growth factor (EGF) receptor ligands in an amount sufficient to stimulate proliferation of the precursor cells. The methods of treatment include transplanting either undifferentiated precursor cells and providing the pancreatic differentiation agent either alone or in combination with the cell expansion agent in situ, or transplanting the functional pancreatic islet  $\beta$ -cells into the patient. The pancreatic islet  $\beta$ -cells can be used for drug screening, and replenishing pancreatic function in the context of clin. treatment.

IC ICM A61K-0048/00

ICS C12N-0005/08

INCL 424093210; X43-536.6

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 2, 9

IT Animal tissue culture  
**Antidiabetic agents**  
 Cell differentiation  
 Cell immortalization  
**Diabetes mellitus**  
 Human  
**Pancreatic islet of Langerhans**  
 Sus scrofa domestica  
 (islet precursor cell treatment for diabetes)

IT **Pancreatic islet of Langerhans**  
 (transplant; islet precursor cell treatment for diabetes)

IT **Pancreatic islet of Langerhans**  
 ( $\beta$ -cell, precursor; islet precursor cell treatment for diabetes)

IT 39024-57-2  
 RL: BUU (Biological use, unclassified); **PAC (Pharmacological activity)**; BIOL (Biological study); USES (Uses)  
 (human; islet precursor cell treatment for diabetes)

IT 9004-10-8, Insulin, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (pancreatic content of; islet precursor cell treatment for diabetes)

IT 39024-57-2  
 RL: BUU (Biological use, unclassified); **PAC (Pharmacological activity)**; BIOL (Biological study); USES (Uses)  
 (human; islet precursor cell treatment for diabetes)

IT 9004-10-8, Insulin, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (pancreatic content of; islet precursor cell treatment for diabetes)

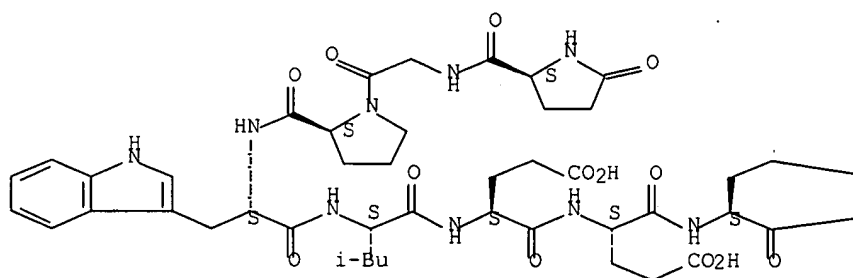
IT 39024-57-2  
 RL: BUU (Biological use, unclassified); **PAC (Pharmacological activity)**; BIOL (Biological study); USES (Uses)  
 (human; islet precursor cell treatment for diabetes)

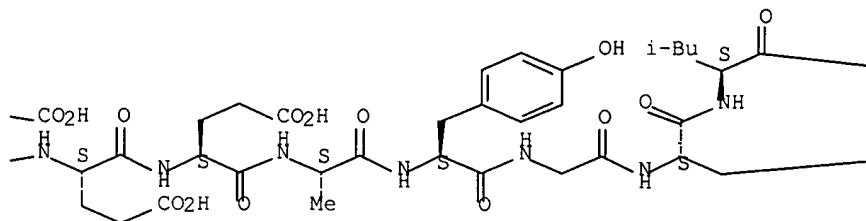
RN 39024-57-2 HCAPLUS

CN Gastrin-17 I (human), 15-L-leucine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO2002055152	A2	20020718	2002WO-US00685	20020111
	WO2002055152	C1	20021114		
	WO2002055152	C2	20030123		
	WO2002055152	A3	20030410		
	W: AU, CA, CN, HU, IL, IN, JP, KR, NO, PH, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				
	PT, SE, TR				
	CA---2434330	AA	20020718	2002CA-2434330	20020111
	US2002098178	A1	20020725	2002US-0044048	20020111
	US---6992060	B2	20060131		
	EP---1351742	A2	20031015	2002EP-0708990	20020111
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, FI, CY, TR				
	JP2004520345	T2	20040708	2002JP-0555881	20020111
	ZA2003005347	A	20041011	2003ZA-0005347	20030710
	US2006234932	A1	20061019	2005US-0273615	20051114
PRAI	2001US-261638P	P	20010112		

2002US-0044048            A1     20020111  
2002WO-US00685            W     20020111

AB    Compns. and methods are provided for achieving in vivo islet cell regeneration in subjects with preexisting diabetes. The methods comprise short term treatment with a composition having a gastrin/cholecystokinin receptor ligand and an EGF receptor ligand. Treatment with such a composition for a short term resulted in a prolonged period of increased insulin release, decreased fasting blood glucose, and improved glucose tolerance, the prolonged efficacy, the period being considered from the time of cessation of treatment.

IC    ICM   A61P-0003/10

ICS   A61K-0045/06

CC    1-10 (Pharmacology)

Section cross-reference(s): 2, 63

IT    **Antidiabetic agents**

**Diabetes mellitus**

      Drug delivery systems

      Human

      Mammalia

**Pancreatic islet of Langerhans**

      Primates

      Rodentia

      (gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

IT    **Diabetes mellitus**

      (insulin-dependent; gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

IT    **Diabetes mellitus**

      (non-insulin-dependent; gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

IT    **Pancreatic islet of Langerhans**

      ( $\beta$ -cell; gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

IT    50-99-7, D-Glucose, biological studies 9004-10-8,

      Insulin, biological studies

      RL: BSU (Biological study, unclassified); BIOL (Biological study)

      (gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

IT    9002-76-0D, Gastrin, derivs. 39024-57-2    60748-06-3, Gastrin 17

      62229-50-9D, EGF, derivs.    442701-38-4

      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

      (gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

IT    50-99-7, D-Glucose, biological studies 9004-10-8,

      Insulin, biological studies

      RL: BSU (Biological study, unclassified); BIOL (Biological study)

      (gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

IT    39024-57-2

      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

      (gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

IT    50-99-7, D-Glucose, biological studies

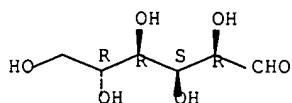
      RL: PAC (Pharmacological activity); THU (Therapeutic use)

      (gastrin/CCK receptor ligand and EGF receptor ligand composition for islet neogenesis in subjects with preexisting diabetes)

RN    50-99-7    HCAPLUS

CN    D-Glucose (8CI, 9CI)    (CA INDEX NAME)

Absolute stereochemistry.



=> d bib abs hitind hitstr retable 158 tot

L58 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:872805 HCAPLUS Full-text

DN 141:360689

TI Treatment of gastrointestinal diseases by modulating gastrin activity

IN Baldwin, Graham S.; Barnham, Kevin Jeffrey; Pannequin, Julie; Tantiongco, John-Paul; Shulkes, Arthur; Norton, Raymond Stanley; Kovak, Suzana; He, Hong; Shehan, Brian Philip

PA The University of Melbourne, Australia; The Walter and Eliza Hall Institute of Medical Research

SO PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2004089976	A1	20041021	2004WO-AU00474	20040408
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU2004228087	A1	20041021	2004AU-0228087	20040408
PRAI	2003US-461083P	P	20030408		
	2004WO-AU00474	W	20040408		

AB This invention relates to methods and compns. for the treatment of conditions associated with abnormal activity or secretion of the hormone gastrin. In particular the invention relates to the treatment of conditions associated with non-amidated gastrin. In one aspect there is provided a method of treatment or prophylaxis of a condition associated with elevated levels of non-amidated gastrin, comprising the step of administering to a mammal in need of such treatment an effective amount of a compound which has the ability to inhibit the binding of ferric ions to any one or more of glycine-extended gastrin17 or progastrin or progastrin-derived peptides, but which does not inhibit the activity of amidated gastrin, thereby to inhibit the activity of non-amidated gastrins.

IC ICM C07K-0007/06

ICS C07K-0007/08; C07K-0014/595; A61K-0033/24; A61P-0001/00; A61P-0035/00

CC 1-9 (Pharmacology)

Section cross-reference(s): 2

IT **Pancreatic islet of Langerhans**

(carcinomas; treatment of gastrointestinal diseases by modulating gastrin activity)

IT 67763-97-7, IGF-2

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(imprinting of; treatment of gastrointestinal diseases by modulating gastrin activity)

IT 55592-74-0 57738-22-4 100304-54-9 108093-87-4 114932-20-6

765956-33-0 765956-34-1 765956-35-2

RL: PRP (Properties)

(unclaimed sequence; treatment of gastrointestinal diseases by  
modulating gastrin activity)

IT 67763-97-7, IGF-2

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(imprinting of; treatment of gastrointestinal diseases by modulating  
gastrin activity)

RN 67763-97-7 HCAPLUS

CN Insulin-like growth factor II (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 108093-87-4

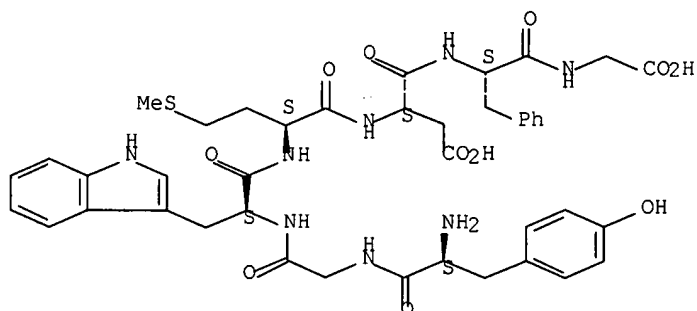
RL: PRP (Properties)

(unclaimed sequence; treatment of gastrointestinal diseases by  
modulating gastrin activity)

RN 108093-87-4 HCAPLUS

CN Glycine, L-tyrosylglycyl-L-tryptophyl-L-methionyl-L- $\alpha$ -aspartyl-L-  
phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



#### RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bower, J	1974	160	1820	Biochemical and Biop	HCAPLUS
Gregory, R	1979	1360	173	Hoppe-Seyler's Z Phy	HCAPLUS
Kneib-Cordonier, N	1990	135	1527	International Journa	HCAPLUS

L58 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:594712 HCAPLUS Full-text

DN 137:150267

TI Methods using pyrazine compounds and pyridine compounds for inhibiting JAK  
kinases, compound preparation, and therapeutic use

IN Burns, Christopher John; Wilks, Andrew Frederick

PA Cytopia Pty. Ltd., Australia

SO PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI WO2002060492	A1	20020808	2002WO-AU00089	20020130
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,				

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA---	2436487	AA	20020808	2002CA-2436487	20020130
EP---	1363702	A1	20031126	2002EP-0715984	20020130

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP2004528295	T2	20040916	2002JP-0560683	20020130
US2004102455	A1	20040527	2003US-0470955	20030730
US2006069084	A1	20060330	2005US-0223633	20050909

PRAI 2001AU-0002792 A 20010130  
2001AU-0002793 A 20010130  
2002WO-AU00089 W 20020130  
2003US-0470955 A3 20030730

OS MARPAT 137:150267

AB The invention provides methods of inhibiting JAK kinases involving the use of a group of compds. based either upon a 2-amino-6-carba-disubstituted pyrazine scaffold or a 2-amino-6-carba-disubstituted pyridine scaffold. The invention also provides methods of treating JAK-associated disease states.

IC ICM A61K-0031/435  
ICS A61K-0031/443; A61K-0031/4436; A61K-0031/4439; A61K-0031/444;  
A61K-0031/496; A61K-0031/497; A61K-0031/4985; A61K-0031/5377;  
A61K-0031/551; A61P-0007/12; A61P-0011/02; A61P-0017/00;  
A61P-0019/00; A61P-0031/12; A61P-0035/00; A61P-0035/02

CC 1-12 (Pharmacology)  
Section cross-reference(s): 28

IT **Diabetes mellitus**  
(insulin-dependent; pyrazine compds. and pyridine compds. for  
inhibiting JAK kinases, compound preparation, and therapeutic use)

IT Allergy inhibitors  
Alzheimer's disease  
Anti-Alzheimer's agents  
Antiarthritics  
Antiasthmatics  
**Antidiabetic agents**  
Antirheumatic agents  
Antitumor agents  
Antiviral agents  
Autoimmune disease  
Eczema  
Hepatitis B virus  
Hepatitis C virus  
Human  
Human T-lymphotropic virus 1  
Human herpesvirus 3  
Human herpesvirus 4  
Human immunodeficiency virus  
Human papillomavirus  
Rheumatic diseases  
Rheumatoid arthritis  
Sjogren syndrome  
(pyrazine compds. and pyridine compds. for inhibiting JAK kinases,  
compound preparation, and therapeutic use)

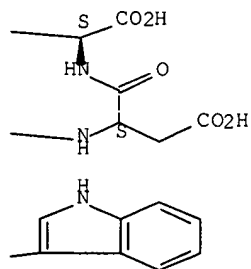
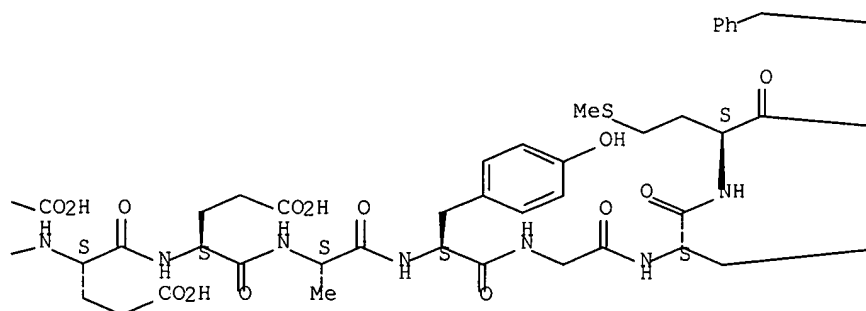
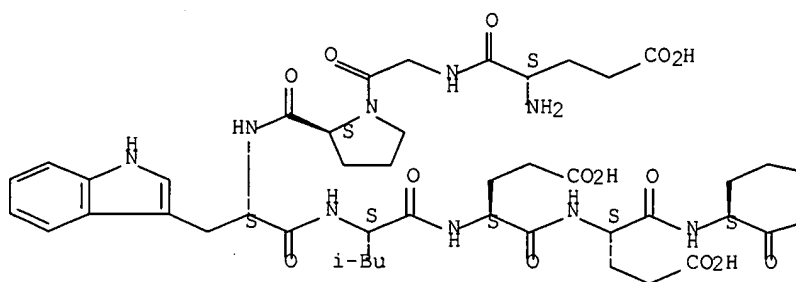
IT 101214-33-9  
RL: PRP (Properties)  
(unclaimed sequence; methods using pyrazine compds. and pyridine  
compds. for inhibiting JAK kinases, compound preparation, and therapeutic use)

IT 101214-33-9  
RL: PRP (Properties)  
(unclaimed sequence; methods using pyrazine compds. and pyridine  
compds. for inhibiting JAK kinases, compound preparation, and therapeutic use)

RN 101214-33-9 HCAPLUS

CN 18-34-Gastrin I (swine), 18-L-glutamic acid-22-L-leucine-34-L-  
phenylalanine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



## RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Bonnet, P	1992	35	3353	Journal of Medicinal	HCAPLUS
Merck & Co Inc	1989			EP---0340836 A	HCAPLUS
Merck & Co Inc	2001			AU--A7351700	
Ono Pharm Co Ltd	1997			JP--09132529 A	HCAPLUS
Regnier, G	1974			US---3821225 A	HCAPLUS

L58 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:713586 HCAPLUS Full-text

DN 135:269070

TI Multifunctional proteins binding to NKG2D receptor complex and their use



in treatment of cancer, infections, and autoimmune diseases  
IN Kufer, Peter; Riethmüller, Gert; Lutterbuese, Ralf; Borschert, Katrin;  
Kischel, Roman; Mayer, Monika; Hofmeister, Robert  
PA Germany  
SO PCT Int. Appl., 114 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2001071005	A2	20010927	2001WO-EP03414	20010326
	WO2001071005	A3	20020103		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,				
	HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,				
	LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,				
	RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,				
	VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				
	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				
	BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA---2406993	AA	20010927	2001CA-2406993	20010326
	EP---1266014	A2	20021218	2001EP-0933752	20010326
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP2004500108	T2	20040108	2001JP-0569387	20010326
	NO2002004489	A	20021119	2002NO-0004489	20020919
	US2004038339	A1	20040226	2003US-0239656	20030107
PRAI	2000EP-0106467	A	20000324		
	2001WO-EP03414	W	20010326		

AB The present invention relates to a multifunctional polypeptide comprising a first domain comprising a binding site specifically recognizing an extracellular epitope of the NKG2D receptor complex and a second domain having receptor or ligand function. Furthermore, the present invention relates to polynucleotides encoding the multifunctional polypeptide, to vectors comprising said polypeptides and to cells comprising said polynucleotides or said vectors. The invention also relates to compns. comprising either of the above recited mols., alone or in combination, as well as to specific medical uses of the multifunctional polypeptide of the invention. Thus, scFv proteins binding to NKG2D and Ep-CAM were produced. These scFv's recruited cytotoxic lymphocytes (CD8+ T cells and NK cells) and caused lysis of Ep-CAM-producing cells.

IC ICM C12N-0015/62  
ICS C07K-0019/00; C12N-0015/85; C12N-0005/10; A61K-0039/395;  
A61K-0047/48; A61K-0038/17; A61K-0048/00; A61P-0031/00; A61P-0035/00;  
A61P-0037/00; G01N-0033/53; C12Q-0001/68; C07K-0014/705;  
C07K-0016/28; C07K-0016/46; C07K-0014/47

CC 6-3 (General Biochemistry)  
Section cross-reference(s): 1, 3, 15

IT **Diabetes mellitus**  
(insulin-dependent; multifunctional proteins binding to NKG2D receptor complex and their use in treatment of cancer, infections, and autoimmune diseases)

IT	153288-60-9	155661-32-8	162290-70-2	192433-87-7	192705-48-9
	266689-50-3	333303-31-4	362457-07-6	363564-18-5	363564-19-6
	363564-20-9	363564-21-0	363564-22-1	363564-23-2	363564-24-3
	363564-25-4	363564-26-5	363564-27-6	363564-28-7	363564-29-8
	363564-30-1	363564-31-2	363636-48-0		

RL: PRP (Properties)

(unclaimed sequence; multifunctional proteins binding to NKG2D receptor complex and their use in treatment of cancer, infections, and autoimmune diseases)

IT 363564-30-1

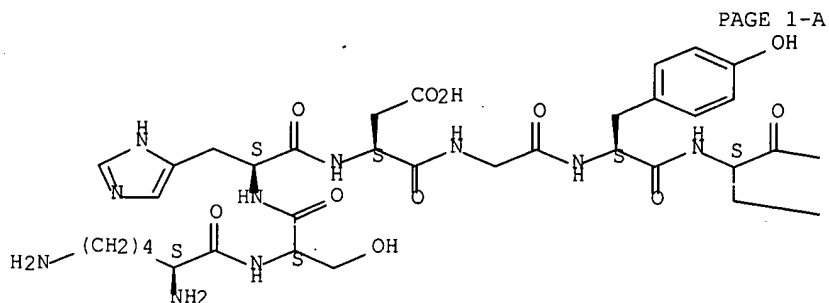
RL: PRP (Properties)

(unclaimed sequence; multifunctional proteins binding to NKG2D receptor complex and their use in treatment of cancer, infections, and autoimmune diseases)

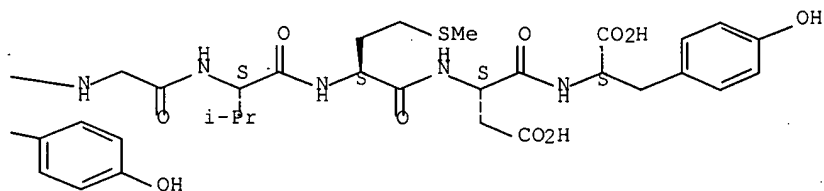
RN 363564-30-1 HCAPLUS

CN L-Tyrosine, L-lysyl-L-seryl-L-histidyl-L- $\alpha$ -aspartylglycyl-L-tyrosyl-L-tyrosylglycyl-L-valyl-L-methionyl-L- $\alpha$ -aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B



L58 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 1995:340887 HCAPLUS Full-text

DN 122:131007

TI Immunogenic LHRH peptide constructs and synthetic universal immune stimulators for vaccines

IN Ladd, Anna E.; Wang, Chang Yi; Zamb, Timothy

PA USA

SO PCT Int. Appl., 217 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO---9425060	A1	19941110	1994WO-US04832	19940428
W: AU, CA, FI, JP, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA---2161445	AA	19941110	1994CA-2161445	19940428
AU---9466702	A1	19941121	1994AU-0066702	19940428
AU---687805	B2	19980305		
EP---708656	A1	19960501	1994EP-0915447	19940428
EP---708656	B1	20020731		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP--09503742	T2	19970415	1994JP-0524614	19940428
JP---3795914	B2	20060712		
AT---221387	E	20020815	1994AT-0915447	19940428
ES---2180576	T3	20030216	1994ES-0915447	19940428
US---5843446	A	19981201	1995US-0488351	19950607

	FI---	9505101	A	19951221	1995FI-0005101	19951026
	NO---	9504279	A	19951227	1995NO-0004279	19951026
	NO---	316121	B1	20031215		
	US---	5759551	A	19980602	1995US-0446692	19951226
	JP2005060406		A2	20050310	2004JP-0293637	20041006
PRAI	1993US-0057166		A	19930427		
	1994US-0229275		A	19940414		
	1994JP-0524614		A3	19940428		
	1994WO-US04832		W	19940428		
	1995US-0446692		A3	19950605		
	1995US-0488351		A3	19950607		

AB This invention relates to immunogenic LH releasing hormone (LHRH) peptides that lead to suppression of LHRH activity in males or females. When male rats are immunized with these peptides, serum testosterone drops and androgen-dependent organs atrophy significantly. These peptides are useful for inducing infertility and for treating prostatic hyperplasia, androgen-dependent carcinoma, prostatic carcinoma and testicular carcinoma in males. In females, the peptides are useful for treating endometriosis, benign uterine tumors, recurrent functional ovarian cysts and (severe) premenstrual syndrome as well as prevention or treatment of estrogen-dependent breast cancer. The subject peptides contain a helper T cell epitope and have LHRH at the C terminus. The helper T cell epitope aids in stimulating the immune response against LHRH. The peptides, optionally contain an invasin domain which acts as a general immune stimulator. In another aspect this invention relates to immunogenic synthetic peptides having an invasin domain, a helper T cell epitope and a peptide hapten and methods of using these peptides to treat disease or provide protective immunity. The peptide haptens of the invention include LHRH, amylin, gastrin, gastrin releasing peptide, IgE CH4 peptide, Chlamydia MOMP peptides, HIV V3 peptides and Plasmodium berghei.

IC ICM A61K-0037/38

ICS A61K-0037/02; A61K-0037/43; A61K-0037/04; A61K-0039/395

CC 15-2 (Immunochemistry)

Section cross-reference(s): 1, 63

IT Allergy inhibitors

**Antidiabetics and Hypoglycemics**

Immunostimulants

Ulcer inhibitors

Vaccines

(immunogenic constructs containing helper T cell epitope fused to LHRH and synthetic universal immune stimulators for vaccines)

IT 70669-29-3 ' 93755-85-2, Gastrin-releasing peptide (human) 109708-37-4

121341-10-4 122384-88-7 160824-89-5 160824-90-8 160824-91-9

160824-92-0 160824-93-1 **160824-94-2** 160824-95-3

160824-96-4 160824-97-5 160824-98-6 160824-99-7 160829-46-9

160830-66-0 160830-67-1 160830-68-2 160830-69-3 160830-70-6

160830-71-7 160830-72-8 160830-73-9 161076-38-6 161076-39-7

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(immunogenic constructs containing helper T cell epitope fused to hapten for vaccines)

IT **160824-94-2**

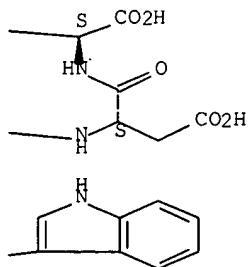
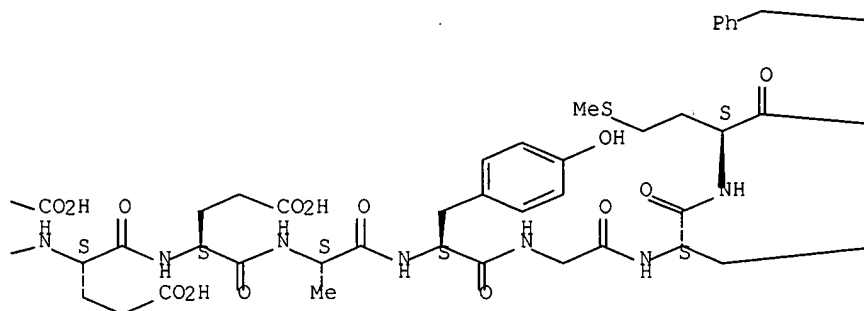
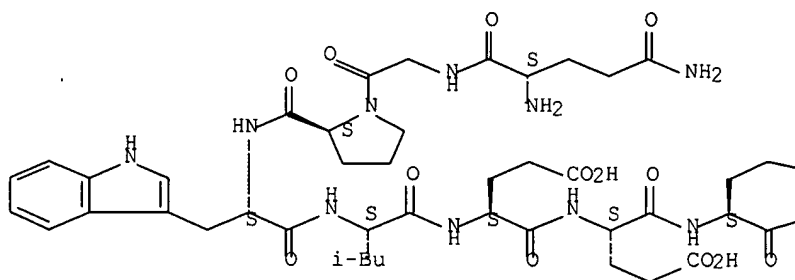
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(immunogenic constructs containing helper T cell epitope fused to hapten for vaccines)

RN 160824-94-2 HCAPLUS

CN Gastrin-17 I (human), 1-L-glutamine-17-L-phenylalanine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L58 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 1992:144071 HCAPLUS Full-text

DN 116:144071

TI Cat gastrinoma and the sequence of cat gastrins

AU Eng, John; Du, Bao Heng; Johnson, Gerald F.; Kanakamedala, Satish; Samuel, Shelby; Raufman, Jean Pierre; Straus, Eugene

CS Health Sci. Cent., State Univ. New York, Brooklyn, NY, 11203-2098, USA

SO Regulatory Peptides (1992), 37(1), 9-13

CODEN: REPPDY; ISSN: 0167-0115

DT Journal

LA English

AB Following the curative resection of a pancreatic gastrinoma in a cat, gastrin peptides were purified from the tissue and sequenced. The sequence of cat gastrinoma G17 (18-

34) confirms the previously published sequence. The sequence of cat G34 (1-34) is reported for the 1st time. The NH<sub>2</sub>-terminal portion of cat G34 differs from that of dog by having a Q (Gln) for L (Leu) at position 10 from the NH<sub>2</sub>-terminus.

CC 2-2 (Mammalian Hormones)

IT **Pancreatic islet of Langerhans**

(neoplasm, gastrinoma, gastrin from, of cat, amino acid sequence of)

IT **27686-19-7** 139246-69-8

RL: PRP (Properties)

(amino acid sequence of, complete)

IT **27686-19-7**

RL: PRP (Properties)

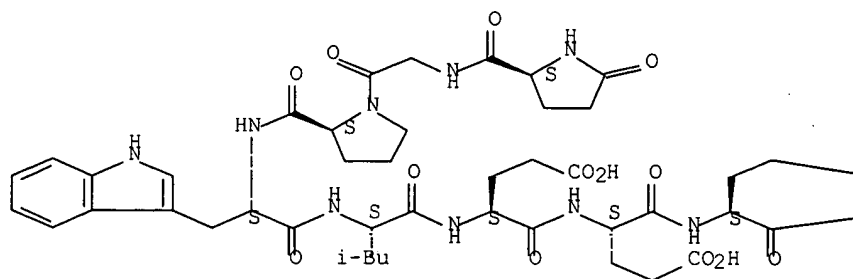
(amino acid sequence of, complete)

RN 27686-19-7 HCAPLUS

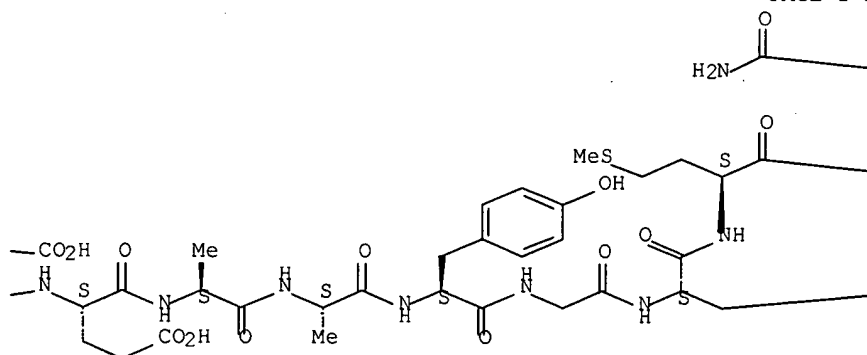
CN Gastrin-17 I (Felis catus) (9CI) (CA INDEX NAME)

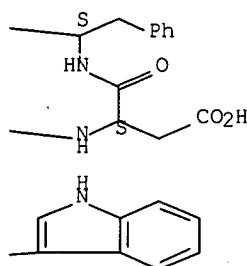
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





L58 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 1978:146676 HCAPLUS Full-text

DN 88:146676

TI The effect of gastrin on basal and amino acid-stimulated insulin and glucagon secretion in man

AU Rehfeld, Jens F.; Holst, Jens J.; Kuhl, Claus

CS Inst. Med. Biochem., Univ. Aarhus, Aarhus, Den.

SO European Journal of Clinical Investigation (1978), 8(1), 5-9  
CODEN: EJCIB8; ISSN: 0014-2972

DT Journal

LA English

AB I.v. injection of human gastrin I (I) [10047-33-3] in doses from 15.6 ng to 1 µg/kg increased the concentration of glucagon [9007-92-5] and insulin [9004-10-8] in peripheral venous blood to a maximum within 5 min. In spite of the enhanced concns. of insulin induced by I, corresponding concns. of glucose were either unchanged or increased. Infusion of a mixture of 15 amino acids increased the concentration of glucose, glucagon, and insulin. While the increases in glucose and insulin concns. were similar to those obtained after a protein-rich meal, the glucagon response was much larger after the infusion. Injection of I after 30 min of infusion of amino acids did not potentiate either the glucagon or the insulin response. Thus, I, besides stimulating insulin secretion, can also stimulate glucagon secretion in a dose-dependent manner. The concns. of I necessary to stimulate glucagon secretion corresponded to the concns. found in diseases with endogenous hypergastrinemia (achlorhydria and Zollinger-Ellison syndrome). Although I potentiates the glucose-induced insulin secretion, it does not potentiate either the amino acid-induced insulin or glucagon secretion.

CC 2-6 (Hormone Pharmacology)

IT 10047-33-3

RL: BIOL (Biological study)

(pancreatic hormone secretion response to, amino acids in relation to)

IT 9004-10-8, biological studies 9007-92-5, biological studies

RL: BIOL (Biological study)

(secretion of, gastrin effect on, amino acids in relation to)

IT 10047-33-3

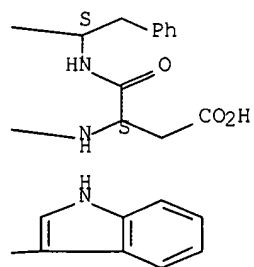
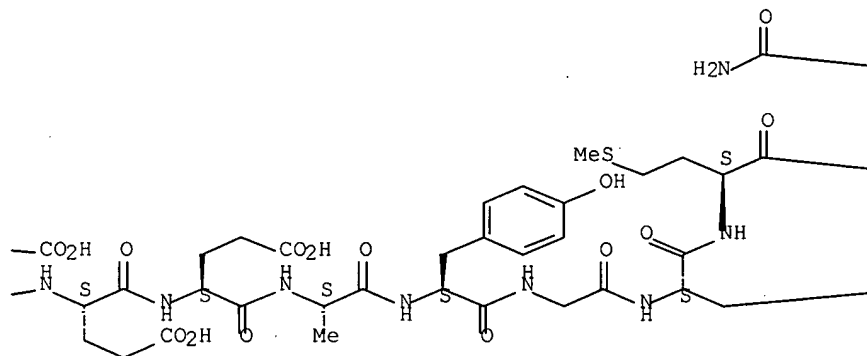
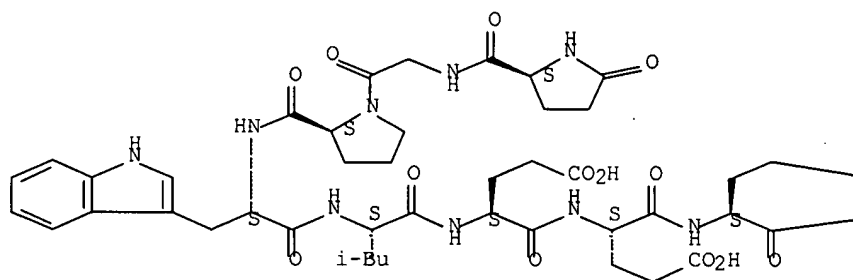
RL: BIOL (Biological study)

(pancreatic hormone secretion response to, amino acids in relation to)

RN 10047-33-3 HCAPLUS

CN Gastrin-17 I (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9004-10-8, biological studies  
 RL: BIOL (Biological study)  
 (secretion of, gastrin effect on, amino acids in relation to)  
 RN 9004-10-8 HCAPLUS  
 CN Insulin (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

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L59 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Herold, K	2005	54	1763	DIABETES	HCAPLUS
Herold, K	2002	346	1692	NEW ENGLAND JOURNAL	HCAPLUS
Keymeulen, B	2005	352	2598	NEW ENGLAND JOURNAL	HCAPLUS
Kuntz, E	2004	5	464	JOURNAL OF THE PANCR	
Mottram, P	2002	10	63	TRANSPLANT IMMUNOLOG	HCAPLUS
Novo Nordisk AS	2003			WO--03105897 A1	HCAPLUS
Waratah Pharmaceuticals	2003			CA---2486584 A1	HCAPLUS
Waratah Pharmaceuticals	2003			CA---2494134 A1	HCAPLUS

L59 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

L59 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Beattie, G	1997	46	244	Diabetes	HCAPLUS
Beattie, G	1999	48	1013	Diabetes	HCAPLUS
Berna, G	2001	55	206	Biomed Pharmacother	HCAPLUS
Bertelli, E	2001	44	575	Diabetologia	HCAPLUS
Bogdani, M	2003	46	830	Diabetologia	MEDLINE
Bonner-Weir, S	1993	42	1715	Diabetes	MEDLINE
Bonner-Weir, S	2000	97	7999	Proc Natl Acad Sci U	HCAPLUS
Bouwens, L	1998	41	629	Diabetologia	MEDLINE
Bouwens, L	1996	427	553	Virchows Arch	MEDLINE
Brand, S	1988	263	5341	J Biol Chem	HCAPLUS
Brand, S	2002	91	414	Pharmacol Toxicol	HCAPLUS
Butler, A	2003	52	102	Diabetes	HCAPLUS
Calnan, D	2000	47	622	Gut	MEDLINE
Cras-Meneur, C	2001	50	1571	Diabetes	HCAPLUS
Dor, Y	2004	429	41	Nature	HCAPLUS
Gao, R	2003	52	2007	Diabetes	HCAPLUS
Gepts, W	1978	27	251	Diabetes	
Gmyr, V	2000	49	1671	Diabetes	HCAPLUS
Gu, D	1993	118	33	Development	HCAPLUS
Halban, P	2004	6	1021	Nat Cell Biol	HCAPLUS
Krakovski, M	1999	162	167	J Endocrinol	HCAPLUS
Lakey, J	1999	8	285	Cell Transplant	MEDLINE
Lechner, A	2003	284	E259	Am J Physiol	HCAPLUS
Miettinen, P	2000	127	2617	Development	HCAPLUS
Paris, M	2003	144	2717	Endocrinology	HCAPLUS
Petersen, B	1981	16	437	Scand J Gastroentero	HCAPLUS
Ramiya, V	2000	6	278	Nat Med	HCAPLUS
Ricordi, C	1988	37	413	Diabetes	MEDLINE
Rooman, I	2002	51	686	Diabetes	HCAPLUS
Rooman, I	2000	43	907	Diabetologia	HCAPLUS
Rooman, I	2002	45	A26	Diabetologia	
Rooman, I	2004	47	259	Diabetologia	HCAPLUS
Ryan, E	2002	51	2148	Diabetes	HCAPLUS
Seaberg, R	2004	22	1115	Nat Biotechnol	HCAPLUS
Serup, P	2001	322	29	Br Med J	MEDLINE
Shapiro, A	2000	343	230	N Engl J Med	HCAPLUS
Si, Z	2001	168	147	Cells Tissues Organs	MEDLINE
Song, S	1999	117	1416	Gastroenterology	MEDLINE
Street, C	2004	53	3107	Diabetes	HCAPLUS
Tourrel, C	2001	50	1562	Diabetes	HCAPLUS
Tyrberg, B	2001	50	301	Diabetes	HCAPLUS
Vinik, A	1996	4	235	Diabet Rev	
Wang, R	1997	40	887	Diabetologia	HCAPLUS
Wang, T	1992	41	114	Diabetes	MEDLINE
Wang, T	1993	92	1349	J Clin Invest	HCAPLUS



Xu, G	1999	48	2270	Diabetes	HCAPLUS
Yamamoto, K	2000	49	2021	Diabetes	HCAPLUS

L59 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

L59 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

L59 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

L59 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

L59 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

L59 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

.=> => d his

(FILE 'HOME' ENTERED AT 16:07:12 ON 24 OCT 2006)

FILE 'HCAPLUS' ENTERED AT 16:07:21 ON 24 OCT 2006

L1 6 (US20040228910 OR US20040209801)/PN OR (US2003-728082 OR US2003  
E CRUZ A/AU  
L2 334 E3-36  
E CRUZ ANTONIO/AU  
L3 47 E3-11  
L4 73 WARATAH/CS,PA

FILE 'REGISTRY' ENTERED AT 16:11:56 ON 24 OCT 2006

FILE 'HCAPLUS' ENTERED AT 16:11:58 ON 24 OCT 2006

L5 TRA L1 1- RN : 85 TERMS

FILE 'REGISTRY' ENTERED AT 16:11:58 ON 24 OCT 2006

L6 85 SEA L5  
L7 18 L6 AND [YF][GAS][WVI][ML][DE][FY]/SQSP  
L8 STR  
L9 STR L8  
L10 3 L9 CSS  
L11 236 L9 CSS FULL  
SAV TEM L11 GAR082B/A  
L12 QUE GPWLEEEEEAY/SQSP  
L13 QUE LGPQGPPHLVADPSKKQGPWLEEEEEAY/SQSP  
L14 216 L12|L13  
L15 49 L11 AND L14  
L16 5 L15 AND L7  
L17 12 'GLP'GPWLEEEEEAYGWLDF/SQSP  
L18 1 L17 AND L6

FILE 'HCAPLUS' ENTERED AT 16:45:00 ON 24 OCT 2006

L19 63 L17  
L20 400 L15  
E ALBUMIN/CT  
E ALBUMINS/CT  
E E3+ALL  
L21 90326 E6+OLD,NT  
E E20+ALL  
L22 27842 E6+OLD,NT  
L23 3 L17 AND L21-22.  
L24 2 L23 AND L1-4  
L25 1 L23 NOT L24  
L26 3 L23-25  
E DIABETES/CT  
E E3+ALL  
L27 10753 E1  
E E2+ALL  
L28 12908 E5+OLD

E DIABETES MELLITUS/CT  
 E E3+ALL  
 L29 75124 E15  
 E PANCREATIC ISLET OF LANGERHANS/CT  
 E E3+ALL  
 L30 21762 E10  
 E E21+ALL  
 E ANTIDIABETIC/CT  
 E E4+ALL  
 L31 26127 E3+OLD,NT  
 E E20+ALL  
 L32 11415 E4+OLD  
 E E12+ALL  
 L33 113227 E4+NT

FILE 'REGISTRY' ENTERED AT 16:55:29 ON 24 OCT 2006  
 L34 10044 INSULIN

FILE 'HCAPLUS' ENTERED AT 16:55:37 ON 24 OCT 2006  
 L35 142415 L34  
 L36 195370 GLUCOSE+OLD,NT/CT

FILE 'REGISTRY' ENTERED AT 16:55:59 ON 24 OCT 2006  
 L37 2 GLUCOSE/CN  
 L38 2272 C6H12O6  
 L39 648 L38 AND (OC4 OR OC5)/ES  
 L40 1624 L38 NOT L39  
 L41 238 L39 AND (GLUCOPYRANOS? OR GLUCOFURAN?)  
 L42 215 L41 NOT (MXS/CI OR MIXT)  
 L43 714 L40 AND GLUCOS?

FILE 'HCAPLUS' ENTERED AT 16:57:42 ON 24 OCT 2006  
 L44 QUE L42-43  
 L45 28 L15 AND L27-33,L35-36,L44  
 L46 9 L45 AND L15 (L) (PAC OR DMA OR THU)/RL  
 L47 8 L46 AND L1-4  
 L48 1 L46 NOT L47

FILE 'REGISTRY' ENTERED AT 17:02:13 ON 24 OCT 2006  
 L49 172 L11 AND (LEUCYL? OR GLYCY? OR PROLY? OR GLUTAMIN? OR HISTIDIN?

FILE 'HCAPLUS' ENTERED AT 17:04:24 ON 24 OCT 2006  
 L50 484 L49  
 L51 29 L50 AND L27-33,L35-36,L44  
 L52 5 L51 AND L1-4  
 L53 24 L51 NOT L52  
 L54 1 L53 AND L50 (L) (PAC OR DMA OR THU)/RL  
 L55 23 L53 NOT L54  
 SEL AN 22 L55  
 L56 1 E1-2 AND L55  
 L57 5 L27-32 AND L53  
 L58 6 L56-57  
 L59 9 L26,L47-48,L52

FILE 'MEDLINE' ENTERED AT 17:13:31 ON 24 OCT 2006  
 L60 4 L15  
 L61 11 L49  
 L62 4 L17  
 L63 15 L60-62

FILE 'EMBASE' ENTERED AT 17:15:27 ON 24 OCT 2006  
 L64 1 L63

FILE 'BIOSIS' ENTERED AT 17:15:46 ON 24 OCT 2006  
 L65 10 L63

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